REMARKS

Claims 22-25 and 33-39 are pending in the present application. Claims 22-25 and 33-35 have been amended. Claims 1-21 and 26-32 have been cancelled. No new matter has been added by way of the above amendments. As such, entry and consideration of the amendments is respectfully requested. Claims 33-34 remain withdrawn.

Restriction of the claims

Claims 27-32, 35-39 and the non-elected subject matter of claims 21, 26 and 33-34 remain withdrawn. Applicants request rejoinder 35-39 drawn to methods of using the elected subject matter, upon a finding of novelty and unobviousness of the elected claims.

Rejections under 35 U.S.C. §102

Claims 21-26 and 33-34 have been rejected under 35 U.S.C. 102(a) as being anticipated by Christophersen et al. WO 02/39987 supplemented with CA 136:380081.

Claims 22-23 have been rejected under 35 U.S.C.§102 (b) as being anticipated by Christophersen et al. WO 98/47879.

Claims 21-26, 33 and 34 have been rejected under 35 U.S.C.§102 as being anticipated by Dahl et al. WO 00/24707.

Claims 21-26 and 33-34 have been rejected under 35 U.S.C. §102(e) as being anticipated by US 6,297,261; US 6,706,749, US 6,696,475 or WO 2004/012733 supplemented with CA 140:175143.

Claim 21 and 26 has been cancelled, thus rendering any rejection with regard to these claims moot.

Claims 22-23 and 33-34 have been amended to define the A ring system being 2-chloro-phenyl, 2-fluoro-phenyl, 2-trifluoromethyl-phenyl, 2,3-dichloro-phenyl, 2,4,6-trichloro-phenyl, 2,6-dichloro-phenyl, 3,4-dichloro-phenyl, 3-fluoro-4-chloro-phenyl, 3-trifluoromethyl-4-chloro-

phenyl, 3,5-dichloro-phenyl, 3,5-difluoro-phenyl, 3-fluoro-5-trifluoromethyl-phenyl, 3,5-bis-trifluoromethyl-phenyl or 4-chloro-phenyl. Support for the amendments to the further define the A ring system may be found on page 4, lines 20-28. In addition, claim 22 has been amended to define R^2 as being a tetrazol-moiety. Finally, R^3-R^6 have been further defined as R^3, R^5 and R^6 representing hydrogen and R^4 representing -CH=CH-$COOR^b$, -CH_2-CH_2-$COOR^b$, -CO-NR^b-CH_2-$COOR^c$; -CO-NR^bR^c, -CH=CH-CO-NR^bR^c; -CH_2-CH_2-CO-NR^bR^c, piperidylcarbonyl, -NH-CO-R^d or -NH-CO-NH-R^d; wherein R^d is phenyl optionally substituted with one or more substituents independently selected from chloro, fluoro or trifluoromethyl; or phenyl substituted with -CO-NR^bR^c, -CO-NR^b-CH_2-$COOR^c$, or piperidylcarbonyl; wherein R^b and R^c independently are hydrogen or alkyl; or R^3 and R^5 as each representing hydrogen and R^4 and R^6 each representing chloro.

With the above amendments, the claimed subject matter is clearly distinguished from the compounds of any of Christophersen et al. WO 02/39987 supplemented with CA 136:380081; Christophersen et al. WO 98/47879; Dahl et al. WO 00/24707; US 6,297,261; US 6,706,749, US 6,696,475 or WO 2004/012733 supplemented with CA 140:175143. Withdrawal of the rejections is therefore respectfully requested.

Claims 21-26 and 33-34 have been rejected by the Examiner under 35 U.S.C. §102(g) and possibly 35 U.S.C. §102(f) as being directed to the same invention as claims 3 or 13 of US 6,297,261; claim 6 of US 6,706,749 or claim 6 of US 6,695,475. The Examiner asserts that identical inventions are claimed in the respective claims of the indicated patents and instant claims 21-26 and 33-34. Applicants traverse this rejection and withdrawal thereof is respectfully requested. The Examiner is legally incorrect in her position because the instant claims, even prior to amendment, are not identical to the subject matter of the indicated claims of prior issued patents. An issue under 35 U.S.C. §102(f) and/or (g) would not be created by two applications/patents of the same assignee having related but different matter and associated different inventive entities. As such, the "same invention" is not being claimed and the Examiner has failed to provide any substantial basis for a rejection of the claims under 35 U.S.C.§102(f) and/or (g). Withdrawal of the rejection is respectfully requested.

Obviousness-type double patenting

Claims 21-26 and 33-34 have been rejected under the non-statutory doctrine of obviousness-type double patenting as being obvious over claims 1-15 of US 6,297,261; claims 1-18 of US 6,706,749 or claims 1-13 of US 6,696,475.

Applicants traverse these rejections and withdrawal thereof is respectfully requested.

1) *Claims 1-15 of US 6,297,261* – The instantly claimed compounds, as most broadly encompassed by claim 22, differ from the compounds of claims 1-15 of the '261 patent such that the instantly claimed compounds are unobvious over the subject matter of claims 1-15 of the '261 patent. Claim 1 of the '261 patent defines R^1 as being "a heterocyclic acidic functional group", whereas the equivalent position of the instantly claimed compounds have a tetrazoyl in the same position. There is no suggestion or motivation provided for replacing a heterocylic acidic functional group, specifically with a tetrazoyl. In addition, the A ring system of the instant compounds is defined as being one of the selected subgenus of 2-chloro-phenyl, 2-fluoro-phenyl, 2-trifluoromethyl-phenyl, 2,3-dichloro-phenyl, 2,4,6-trichloro-phenyl, 2,6-dichloro-phenyl, 3,4-dichloro-phenyl, 3-fluoro-4-chloro-phenyl, 3-trifluoromethyl-4-chloro-phenyl, 3,5-dichloro-phenyl, 3,5-difluoro-phenyl, 3-fluoro-5-trifluoromethyl-phenyl, 3,5-bis-trifluoromethyl-phenyl or 4-chloro-phenyl. There is no suggestion or motivation provided the making compounds with the selected subgenus of the ring system A. As such, the instantly claimed compounds are not obvious over claims 1-15 of the '261 patent and withdrawal of the rejection is respectfully requested.

2) *Claims 1-18 of US 6,706,749* – The instantly claimed compounds differ from those of claims 1-18 of the '749 patent at least as follows.

Claim 1 of the '749 patent requires that R^3 (corresponding to R^4 of the instant claims) is halogen and R^2, R^4 and R^5 (corresponding respectively to R^3, R^5 and R^6 of the instant claims) be hydrogen. However, with the present claims, when R^4 is a halogen (chloro), R^6 must also be a halogen (chloro). There is no suggestion, nor would it be obvious to replace a hydrogen moiety with a halogen moiety. Alternatively, when R^3, R^5 and R^6 (corresponding to R^2, R^4 and R^5 of the '749 patent) of the instant claims are hydrogen, R^4 is $-CH=CH-COOR^b$, $-CH_2-CH_2-COOR^b$, -

$CO\text{-}NR^b\text{-}CH_2\text{-}COOR^c$; $-CO\text{-}NR^bR^c$, $-CH{=}CH\text{-}CO\text{-}NR^bR^c$; $-CH_2\text{-}CH_2\text{-}CO\text{-}NR^bR^c$, piperidylcarbonyl, $-NH\text{-}CO\text{-}R^d$ or $-NH\text{-}CO\text{-}NH\text{-}R^d$; wherein R^d is phenyl optionally substituted with one or more substituents independently selected from chloro, fluoro or trifluoromethyl; or phenyl substituted with $-CO\text{-}NR^bR^c$, $-CO\text{-}NR^b\text{-}CH_2\text{-}COOR^c$, or piperidylcarbonyl; wherein R^b and R^c independently are hydrogen or alkyl. It would not be obvious to replace a "halogen" with the complex moieties recited for R^4 above.

In addition, the instantly claimed compounds define the A ring system as as being one of the selected subgenus of 2-chloro-phenyl, 2-fluoro-phenyl, 2-trifluoromethyl-phenyl, 2,3-dichloro-phenyl, 2,4,6-trichloro-phenyl, 2,6-dichloro-phenyl, 3,4-dichloro-phenyl, 3-fluoro-4-chloro-phenyl, 3-trifluoromethyl-4-chloro-phenyl, 3,5-dichloro-phenyl, 3,5-difluoro-phenyl, 3-fluoro-5-trifluoromethyl-phenyl, 3,5-bis-trifluoromethyl-phenyl or 4-chloro-phenyl. There is no suggestion or motivation provided the making compounds with the selected subgenus of the ring system A. There is no suggestion of these specifically recited ring system A moieties in the '749 patent. As such, the instantly claimed compounds are significantly different from the genus of compounds encompassed by claims 1-18 of the '749 patent and would not be obvious over such compounds. Withdrawal of the rejection is therefore respectfully requested.

3) *Claims 1-13 of US 6,696,475* – The compounds encompassed by claims 1-13 of the '475 patent define R^1 as a "heterocyclic acidic group". The corresponding moiety of the instantly claims compounds is tetrozoyl. There is no suggestion or motivation provided for replacing a heterocylic acidic functional group, specifically with a tetrazoyl. In addition, the A ring system of the instant compounds is defined as being one of the selected subgenus of 2-chloro-phenyl, 2-fluoro-phenyl, 2-trifluoromethyl-phenyl, 2,3-dichloro-phenyl, 2,4,6-trichloro-phenyl, 2,6-dichloro-phenyl, 3,4-dichloro-phenyl, 3-fluoro-4-chloro-phenyl, 3-trifluoromethyl-4-chloro-phenyl, 3,5-dichloro-phenyl, 3,5-difluoro-phenyl, 3-fluoro-5-trifluoromethyl-phenyl, 3,5-bis-trifluoromethyl-phenyl or 4-chloro-phenyl. There is no suggestion or motivation provided the making compounds with the selected subgenus of the ring system A. As such, the instantly claimed compounds are not obvious over claims 1-13 of the ''475 patent and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §103

Claims 21-26 and 33-34 have been rejected under 35 U.S.C. 103(a) as being obvious over over Dahl et al. US 6,706,749 or US 6,696,475 or Christophersen et al. US 6,297,261 in view of Dahl et al. US 6,706,749 or US 6,696,475 and supplemented with CA 132:308142. . With regard to the rejections over US '749, US '475 and US '261, the instantly claimed invention was commonly owned with US '749, 'US '475 and US '261 at the time of the invention of the claimed subject matter. As such, US '749, 'US '475 and US '261 are not prior art under 35 U.S.C.§103 against the instant application.

Claims 21-26 and 33-34 have been further rejected under 35 U.S.C.§103 as being obvious over Dahl et al. WO 00/24707 or Christophersen et al. WO 98/47879 in view of Dahl et al. WO 00/24707 supplemented by CA 132:308142. Applicants traverse these rejections and withdrawal thereof is respectfully requested.

The present invention is directed to novel diarylurea derivatives useful as chloride channel blockers. The compounds of the present invention have been developed in order to provide novel compounds, which can be used in a method of therapy, such as for the treatment of bone metabolic diseases, responsive to modulation of the mast cell or basophil activity, diseases responsive to inhibition of angiogenesis or sickle cell anemia (page 1, lines 9-13). More particular, the compounds of the present invention has been developed in order to provide more effective and selective compounds with fewer side effects for the treatment of patients with an osteoclast related bone disease such as osteoporosis (page 1, lines 26-28).

Each of the prior art references cited by the Examiner disclose chemical compounds, which have some structural similarity to the instantly claimed compounds (e.g. a similar core). However, any similarly between the prior art compounds and the instantly claimed compounds is not sufficient to render the present compounds obvious. The compounds encompassed in the revised claims all possess distinct features, which distinguish and render unobvious the presently claimed compounds from the prior art compounds.

The instantly claimed compounds require a very specific and limited substitution on the phenyl of the A ring system. Specifically, the phenyl group can only be substituted with chloro,

fluoro and/or trifluoromethyl in such a way as to form only of 2-chloro-phenyl, 2-fluoro-phenyl, 2-trifluoromethyl-phenyl, 2,3-dichloro-phenyl, 2,4,6-trichloro-phenyl, 2,6-dichloro-phenyl, 3,4-dichloro-phenyl, 3-fluoro-4-chloro-phenyl, 3trifluoromethyl-4-chloro-phenyl, 3,5-dichloro-phenyl, 3,5-difluoro-phenyl, 3fluoro-5-trifluoromethyl-phenyl, 3,5-bis-trifluoromethyl-phenyl or 4-chloro-phenyl.

In addition, the instantly claimed compounds do not include a bromo moiety; the moiety in the R^2 position is a tetrazoyl group; when R^4 is chloro then R^6 must also be chloro (with R^3 and R^6 being hydrogen) and when R^4 is other than chloro and as defined in claim 22, R^3, R^5 and R^6 must be hydrogen.

Christophersen et al. (WO '879) discloses substituted phenyl derivatives, which are potent chloride blockers and, as such, are useful in the treatment of sickle cell anaemia, brain oedema following ischaemia or tumors, diarrhoea, hypertension (diuretic), osteoporosis, and for the reduction of intraocular pressure in the treatment of disorders such as glaucoma. WO'879 discloses on page 27, line 21 through page 28, line 16, compounds having an A ring system, in which the phenyl group may be substituted in the 3-position with trifluoromethyl. This substitution is not included in presently amended claims. Nor is there any suggestion in the prior art of modifying the A ring of WO '879 to achieve the specific substituents recited in the instant claims. As such, the present claims are not obvious over WO '879.

Dahl et al. (WO '707) describes substituted phenyl derivatives, which are potent chloride channel blockers and, as such, are useful in the treatment of sickle cell anaemia, brain oedema following ischaemia or tumors, diarrhea, hypertension (diuretic), bone metabolic disorders, osteoclast associated disorders and for the reduction of intraocular pressure for the treatment of disorders such as glaucoma. Pages 34-36 (claim 6) of WO '707 discloses compounds having an A ring system that is dramatically different from that of the instantly claimed compounds. For example, most of the compounds of WO '707 have a mono-substituted A ring structure. Only one compound (on page 36, line 4) has an A ring similar to that of the instant claims; however this compounds also has a bromo-moiety, which is not permitted with the present compounds.

Thus, the presently claimed compounds are not obvious over either of WO '707 or WO '879 in view of WO '707 and supplemented by CA 132:308142.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D., Reg. No. 40,069 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____

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